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(54) Title: SPAN-Xb GENE AND PROTEIN FOR THE DIAGNOSIS AND TREATMENT OF CANCER

(57) Abstract: The present invention relates to methods for diagnosing cancer in a subject. The method involves obtaining a biological sample from a subject and measuring SPAN-Xb expression level in the biological sample. The SPAN-Xb expression level in the biological sample is compared to the SPAN-Xb expression level in a control sample from a subject devoid of cancer, where a greater SPAN-Xb expression level in the biological sample compared to the SPAN-Xb expression level in the control sample is indicative of the subject having cancer. Methods for monitoring progression/regression of cancer in a subject are also disclosed. The present invention also relates to methods of treating a subject with cancer. The method involves administering to the subject a therapeutically effective amount of an agent capable of eliciting an immunological response against SPAN-Xb protein or specifically recognizing a SPAN-Xb protein, under conditions effective to treat a cancer characterized by cells expressing SPAN-Xb.



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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/27338

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A61K 35/12, 48/00; C12Q 1/68; G01N 33/53, 33/574  
US CL : 424/93.21, 277.1; 435/6, 7.1, 7.23; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/93.21, 277.1; 435/6, 7.1, 7.23; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
WEST, MEDLINE: SPAN-Xb, cancer, diagnosis, overexpression, cancer vaccine.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MASHINO, K. et al. Expression of multiple cancer-testis antigen genes in gastrointestinal and breast carcinomas. Br. J. Cancer. 2001, Vol. 85, No. 5, pages 713-720; see entire document.	1-18
Y,P	SCANLAN, M.J. et al. Cancer/testis antigens: an expanding family of targets for cancer immunotherapy. Immunol. Rev. 2002, Vol. 188, pages 22-32; see entire document.	13-18
Y	ZENDMAN, A.J.W et al. CTp11, a novel member of the family of human cancer/testis antigens. Cancer Res. 15 December 1999, Vol. 59, pages 6223-6229, see entire document.	1-18
Y,P	ZENDMAN, A.J.W et al. The human SPANX multigene family: genomic organization, alignment and expression in male germ cells and tumor cell lines. Gene. 2003, Vol. 309, pages 125-133, see entire document.	1-18
Y	WESTBROOK, V.A. et al. Spermatid-specific expression of the novel X-linked gene product SPAN-X localized to the nucleus of human spermatozoa. Biol. Reproduction. 2000, Vol. 63, pages 469-481, see entire document.	1-18



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

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## INTERNATIONAL SEARCH REPORT

## C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WESTBROOK, V.A. et al. Differential nuclear localization of the cancer/testis-associated protein, SPAN-X/CTp11, in transfected cells and in 50% of human spermatozoa. Biol. Reproduct. 2001, Vol. 64, pages 345-358, see entire document.	1-18
Y,P	WANG, Z. et al. Gene expression and immunologic consequence of SPAN-Xb in myeloma and other hematologic malignancies. Blood. 01 February 2003, Vol. 101, No. 3, pages 955-960, see entire document.	1-18

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/27338

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
- Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-12, drawn to a method for diagnosing cancer.

Group II, claim(s) 13-18, drawn to a method for treating cancer.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of group I is diagnosing cancer.

The special technical feature of group II is treating cancer.

Groups I and II do not share the same or corresponding special technical feature so as to form a single general inventive concept under PCT Rules 13.1 and 13.2.